



PATENT APPLICATION
Attorney Docket No.122536

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

Edith DELLACHERIE et al.

Serial No.: 10/522,333

Filed: January 25, 2005

Group Art Unit: 1615

Examiner: J. PALENIK

For: PARTICLES WHICH ARE SURFACE COATED WITH HYALURONAN OR ONE OF THE DERIVATIVES THEREOF AND THE USE OF SAME AS BIOLOGICAL VECTORS FOR ACTIVE SUBSTANCES

**DECLARATION OF EDITH DELLACHERIE
UNDER 37 CFR 1.132**

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

I, EDITH DELLACHERIE do hereby declare the following:

1. I am one of the inventors of the above-captioned patent application and have been working at the laboratory called *Laboratoire Physique Macromoléculaire* of the CNRS (Centre National de la Recherche Scientifique) for 41 years. I have directed this laboratory during 10 years and I am Emeritus Professor at the *Institut national polytechnique de Lorraine* since 2005.

Please find enclosed my *Curriculum Vitae*.

2. I have reviewed the last Office Action dated November 24, 2009. I realize that the present invention was rejected due to obviousness in view of the US patent 4,904,479 of Illum.

3. It is well known that a hydrophilic polymer cannot adsorb on a hydrophobic solid material except if there is an affinity (low energy bonding) between the two elements. This affinity can be obtained by essentially two kinds of interactions, either of the hydrophobic type (between the hydrophobic material and a hydrophobic part-carrying hydrophilic polymer, in water) or of the ionic type (between a hydrophobic particle bearing charges and a hydrophilic polymer carrying opposite charges). In this case, the adsorption of the polymer remains always superficial and weak, except if there are strong and numerous interactions.

3. To the contrary, during the preparation of the particles according to the invention by the emulsion/evaporation process, the hydrophobic portion of the amphiphilic hyaluronan extends in the solvent of the emulsion, in which are dissolved the organo-soluble polymer chains. The hydrophilic portion of the hyaluronan remains in the aqueous phase. The hydrophobic portion of the hyaluronan and the organo-soluble polymer chains become entangled and this entanglement remains during evaporation of the solvent. The hydrophobic chains carried by amphiphilic hyaluronan are compatible with the particle-constituting hydrophobic polymer, as shown by Differential Scanning Calorimetry analyses. Strong interactions thus exist between the hyaluronan and the particle core due to hydrophobic interactions inside the matrix between entangled chains of particle-constituting hydrophobic polymer and of hydrophobic groups bore by amphiphilic hyaluronan. This is why, the expression “the anchoring of the hyaluronan in the polymeric core” is claimed.

3. It has never been possible to prepare particles according to the invention with non-amphiphilic hyaluronan, which is an indirect proof of the above-mentioned entanglement and anchoring.

4. In my opinion, it is further not possible to produce particles according to the invention by a process different from the process discussed above since the hydrophobic portions of the amphiphilic hyaluronan should extend in the solvent of the emulsion before the evaporation of the solvent, so that these hydrophobic portions are anchored in the core of the particles and not only on the surface of the particles.

4. I have read the Illum patent US 4,904,479. This patent describes a two-steps process wherein the formed particles are subsequently coated. It merely relates to the adsorption of amphiphilic molecules on the surface of particles, this adsorption being obtained by mere contact between the preformed particles and an aqueous solution of polymer. This adsorption does not allow producing particles according to the invention provided with amphiphilic molecules anchored in the core of the particles.

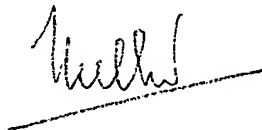
To the contrary, the invention particles both including drugs and coated with a hydrophilic polymer, are prepared in one single step. They are therefore different from the particles produced according to Illum disclosure, and are further more stable as such and there is therefore no need for protein such as gelatine for example to retain the molecules on the surface of the particles.

5. It is my opinion that Illum does not suggest to anchor the amphiphilic molecules in the particles and even to change the method for producing the particles. According to the invention, the amphiphilic molecules are used as surfactant for stabilizing the initial emulsion. The amphiphilic molecules are therefore used for producing the particles which is contrary to the disclosure of Illum according to which the particles are coated after their production.

6. I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of this application or any patent issuing thereon.

February 8, 2010

Date



EDITH DELLACHERIE

CURRICULUM VITAE



GENERAL INFORMATION

Name	Edith DELLACHERIE	Gender : F
Date of birth	02-07-1941	
Institution	National School of Chemical Engineers (ENSIC) — Polytechnic National Institute of Lorraine (INPL) — Nancy-France	
Telephone	33 (0)3 83 17 52 21	
Fax	33 (0)3 83 37 99 77	
E-mail	Edith.Dellacherie@ensic.inpl-nancy.fr	

EDUCATION

1961-1964	Chemical engineer degree at ENSIC — Nancy-France
1964-1971	PhD in Macromolecular Chemistry and Physical Chemistry, in the Laboratory of Macromolecular Physical Chemistry (LCPM)-ENSIC — Nancy-France

WORK EXPERIENCE

1964-1993	CNRS senior researcher in LCPM-ENSIC, CNRS-INPL — Nancy-France
1993-2005	Full professor at ENSIC-INPL
1995-2005	Head of LCPM (about 30 researchers, teachers and technicians ; about 30 PhD students and trainees)
2005-until now	Emeritus Professor-INPL

CONCERN AREAS

Macromolecular chemistry, polymer physical chemistry, biomedical polymers

PUBLICATION ACTIVITY

More than 230 original research papers in refereed international journals
15 patents, French and international.
35 invited lectures in congresses (20 in international ones)